

**FIG.\_1****FIG.\_1A****FIG.\_1B****FIG.\_1A****SEQ ID NO: 1****Nucleotide Sequence Tankyrase Homologue isotype1**

CTTTGAAGACACTGGATTTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA  
TTAGCTGTGAGCAGATCTTTTTTTGTTGCTTCTTGTAGTCCCCCAGTTTAGCAGAAACATTCTGTGAGA  
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA  
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA  
CATTTGAACTTTGAGCTTTCAGTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA  
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGGCG  
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT  
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGGCAGATGGTGCAGA  
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT  
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTGGA  
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC  
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAATGTCAACTGCCACGCAAGTGA  
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT  
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA  
TGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA  
ATTCATCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTTAAAGTTATGG  
TGCAGACCCAACACTGCTCAATTGTGACAATAAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAA  
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG  
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTGCA  
TTGTGCTGCTGCATCTCCATATCCCAAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAA  
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT  
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA

CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACAT  
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGG  
TATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAAAC  
TGTAAAAAAACTGTGTACTGTTTACAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACT  
TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGCTACAGCATGGAGCTGATGTGCA  
TGCTAAAGATAAAGGAGGCCTTGTACCTTTGCACAATGCATGTTCTTATGGACATTATGAAGTTGCAGA  
ACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGC  
AGCAGCAAAGGAAAATATGAAATTTGCAAACCTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAA  
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG  
AGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGA  
TAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAA  
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TCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATG  
TGTCATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCCAAAGGGACGAACACAGCT  
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TTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTG  
TTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTCTTCAGGTCC  
ATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTGGGAGTTTTTCAGAACTGTC  
TTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAAGGAGGTTCAGGAGTAGA  
TTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGGATATATTTGAGAGAGAACA  
GATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG  
ACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTT  
AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC  
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA  
CAGATACAATATTCTCAAGATTCAGAAGGTTTGTAACAAGAACTATGGGAAAGATACACTCACCGGAG  
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTTCATGGGTCTCCTTTTGT  
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT  
TTATTTTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCC  
AGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTTGCCGGGTAACTTGGGAAA  
GTCTTTCTGTCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG  
GCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA  
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAACTA  
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAA  
AA

**FIG. 1B**

**FIG.\_2****FIG.\_2A****FIG.\_2B****FIG.\_2A****SEQ ID NO: 2****Nucleotide Sequence Tankyrase Homologue isotype2**

CGCGCTGCTCCGCCCCGCGGGGCGAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCGTGGGCGCGG  
CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCGGGCCCTGAGCGCGTCTTCTC  
CGGGGGGCGCTCGCCCTCCTGCTCGCGGGGCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG  
TGGCGGCGGCCAGGATCATGTGCGGTGCGCGCTGCGCCGGCGGGGAGCGGCCTGCGCGAGCGCCGCGG  
CCGAGGCCGTGGAGCCGGCCGCCGAGAGCTGTTGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA  
AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCCGCTGCACT  
TCGCCGCGAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC  
GTGATGATGGGGGCGCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC  
TTTTGCGACATGGTGCGAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA  
TTAAAGGAAAGATTGATGTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG  
ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG  
ATGAACTCTTAGAAAGTGCCAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATG  
TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA  
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT  
TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAA  
ATGCAATGGACTTGTGGCAATTCCTCTTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT  
CTCTTCTCTTAAGTTATGGTGCAGACCCCAACTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGG  
CTCCACACACAGTTAAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC  
GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAA  
CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGT  
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTG  
AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATC

TTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCTACTCCTGAGCT  
ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTAC  
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAA  
AGGCTGGAGATGTGCAAACTGTAAAAAACTGTGTACTGTTTCAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTAC  
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGACCTTTGCACAATGCATGTTCTTATG  
GACATTATGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAAT  
TTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATTTGCAAACTTCTGCTCCAGCATGGTG  
CAGACCCTACCAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATA  
TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA  
AGAAGTTGTCTTCTCCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT  
TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC  
AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC  
TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCC  
AAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGG  
AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC  
CATCTGCTCTGCCCTCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAG  
ATGCTCTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTG  
GGAGTTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAA  
AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGAATTGAGCACCTAATGG  
ATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGA  
TTGGAATCAATGCTTATGGACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAAC  
AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG  
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TTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTG  
GTATGTTTGGAGCTGGCATTATTTTGTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTG  
GAGGAGGTACTGGGTGTCCAGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT  
GCCGGGTAACCTTGGGAAAGTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTC  
ATCACTCAGTCACTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG  
AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAA  
TAGTTATTTTAAGAACTAATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTAC  
TCCTTTGCTGAAAAA

**FIG.\_2B**

**SEQ ID NO: 3****Amino Acid Sequence Tankyrase Homologue isotype1**

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFGHAEVVNLLLRHGADPNARDNWNYPPLHEAAIKG  
KIDVCIVLLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNC  
HASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVELLVKHGACVNM  
DLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAPTQPKERLAYEFKGHSLQAAAREA  
DVTRIKKHLSELMVNFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKEFLTPLHVASEKA  
HNDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIISLQGFALQMGNEENVQQL  
LQEGISLGNSEADRQLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG  
ADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGADP  
TKKNRDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA  
GYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG  
RTQLCALLLAHGADPTLKNQEGQTPDLVLSADDVSALLTAAMPSPALPSCYKPQVLNGVRSPGATADAL  
SSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMDIF  
EREQITLDVLVEMGHKELKEIGINAYGHRHKLIGVERLISGQQGLNPYLTNTSGSGTILIDLSPDDK  
EFQSVEEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLFHG  
SPFVNAIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFCRV  
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALA EYVIYRGEQAYPEYLITYQIMRPEGMVDG

**FIG.\_3**

**SEQ ID NO: 4****Amino Acid Sequence Tankyrase Homologue isotype2**

RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV  
AAARIMSGRRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF  
AAGFGRKDVVEYLLQNGANVQARDDGGLIPLHNACSFSGHAEVVNLLLRHGADPNARDNWNYPPLHEAAI  
KGKIDVCIVLLQHGAETIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV  
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGAADVHAKDKGDLVPLHNACSYGHYEVTTELLVKHGACVN  
AMDWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLQAAAR  
EADVTRIKKHLSEMVNFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKFELTPLHVASE  
KAHNDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLLSYGCDPNIISLQGFALQMGNENVQ  
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ  
HGADVHAKDKGGLVPLHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA  
DPTKKNRDGNTPDLVKGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL  
AAGYNNLEVAEYLLQHGAADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ  
KGRTQLCALLLAHGADPTLKNQEGQTPDLVVSADDVSALLTAAMPSPALPSCYKPQVLNGVRSPGATAD  
ALSSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLM  
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLIGVERLISGQQLNPYLTLNTSGSGTILIDLSPD  
DKEFQSVVEEMQSTVREHRDGGHAGGIFNRYNLIKIQVCNKKLWERYTHRRKEVSEENHNHANERMLF  
HGSPFVNAIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC  
RVTLGKSFLQFSAMKMAHSPPGHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

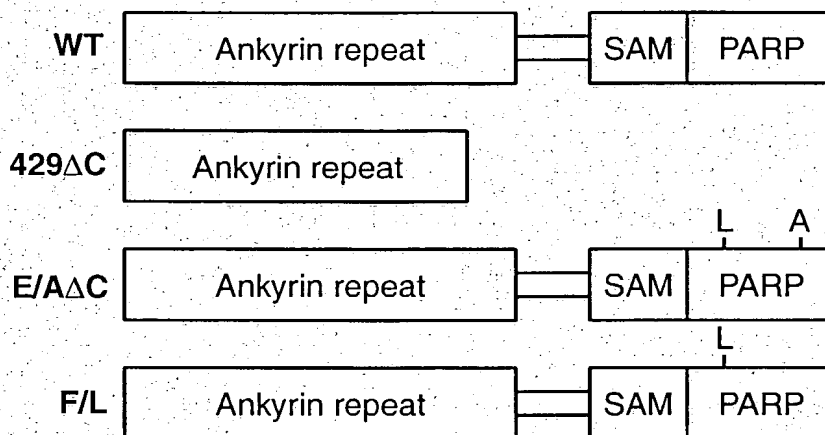
**FIG.\_4**

### Schematic Presentation of Dominant Negative Mutants for Tankyrase Homologue

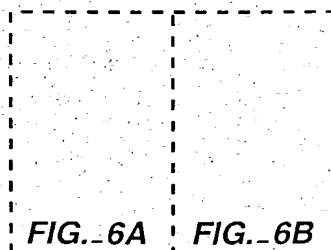
#### Dominant Negative Mutants

Truncation: 429 $\Delta$ C- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25; 18(50):7010-5)

Point mutant: E945A $\Delta$ C- conserved residue in PARP domain, thought to be important in NAD<sup>+</sup> binding



**FIG.\_5**

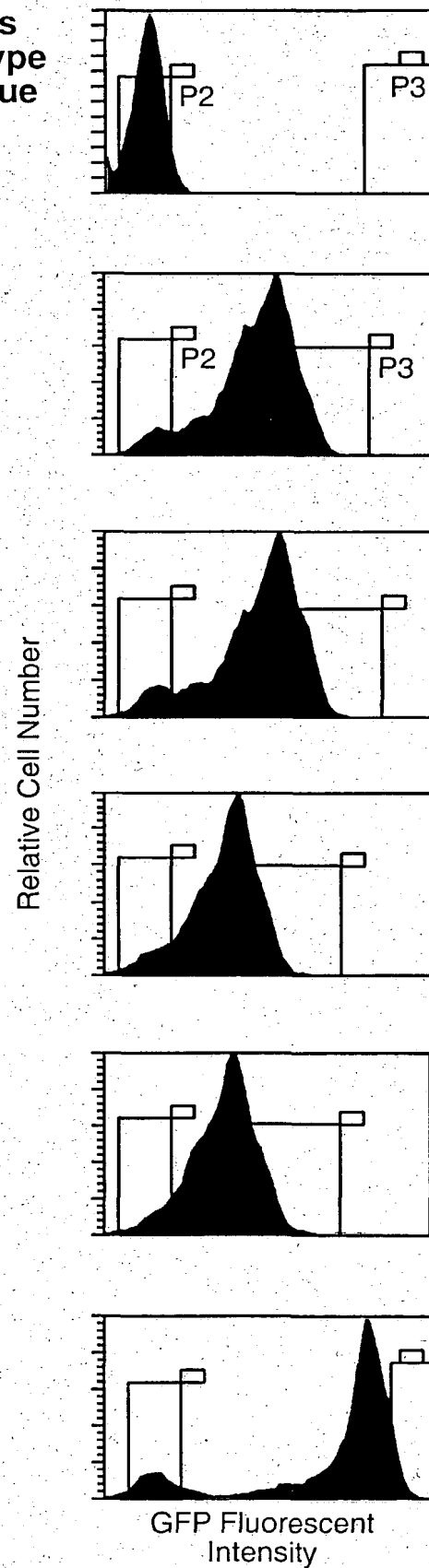


**FIG.\_6**

+

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**Cell Cycle Analysis of A549 Cells  
Infected With GFP-fused Wild Type  
and Mutant Tankyrase Homologue**



**FIG 6A**



A-68292-2

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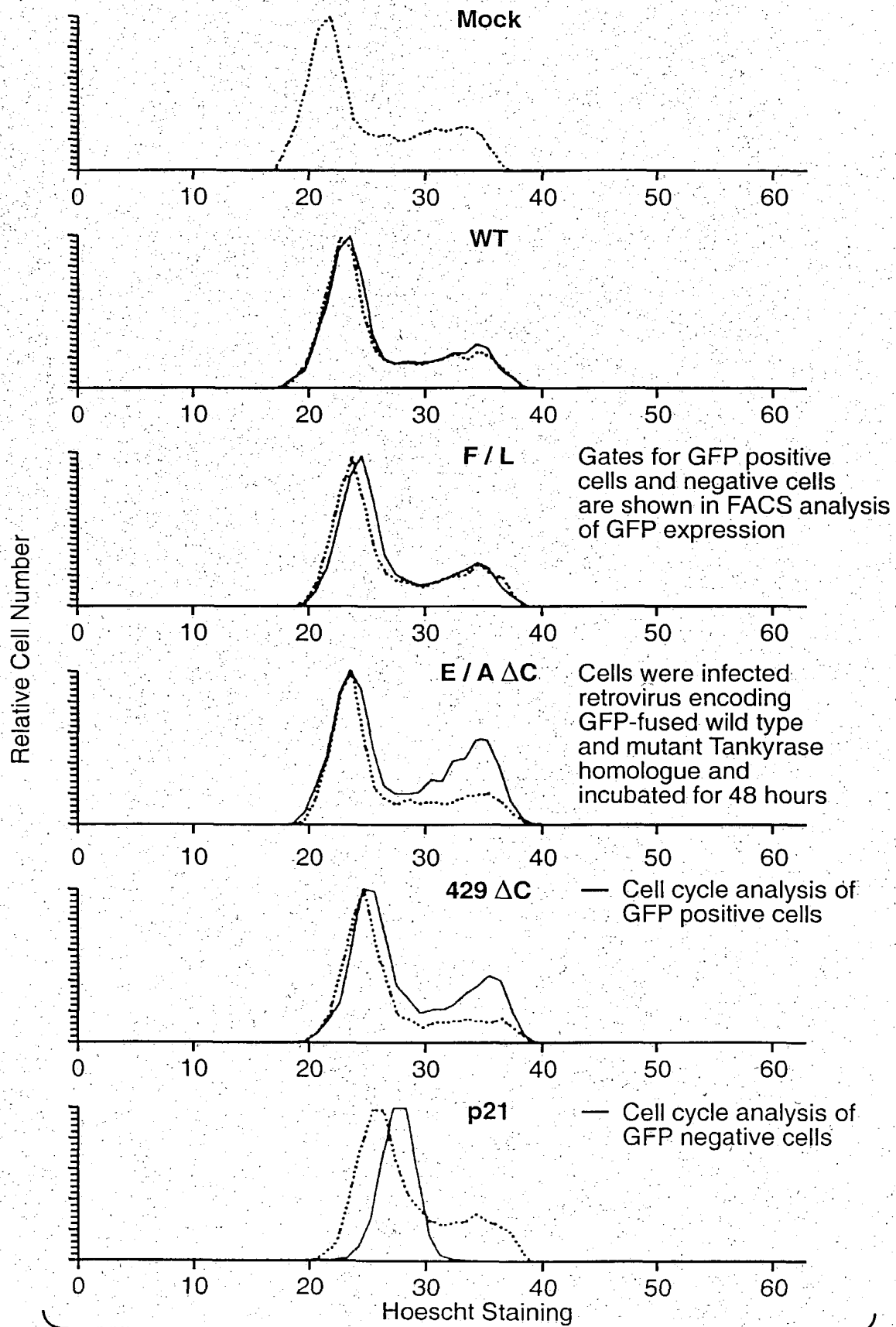
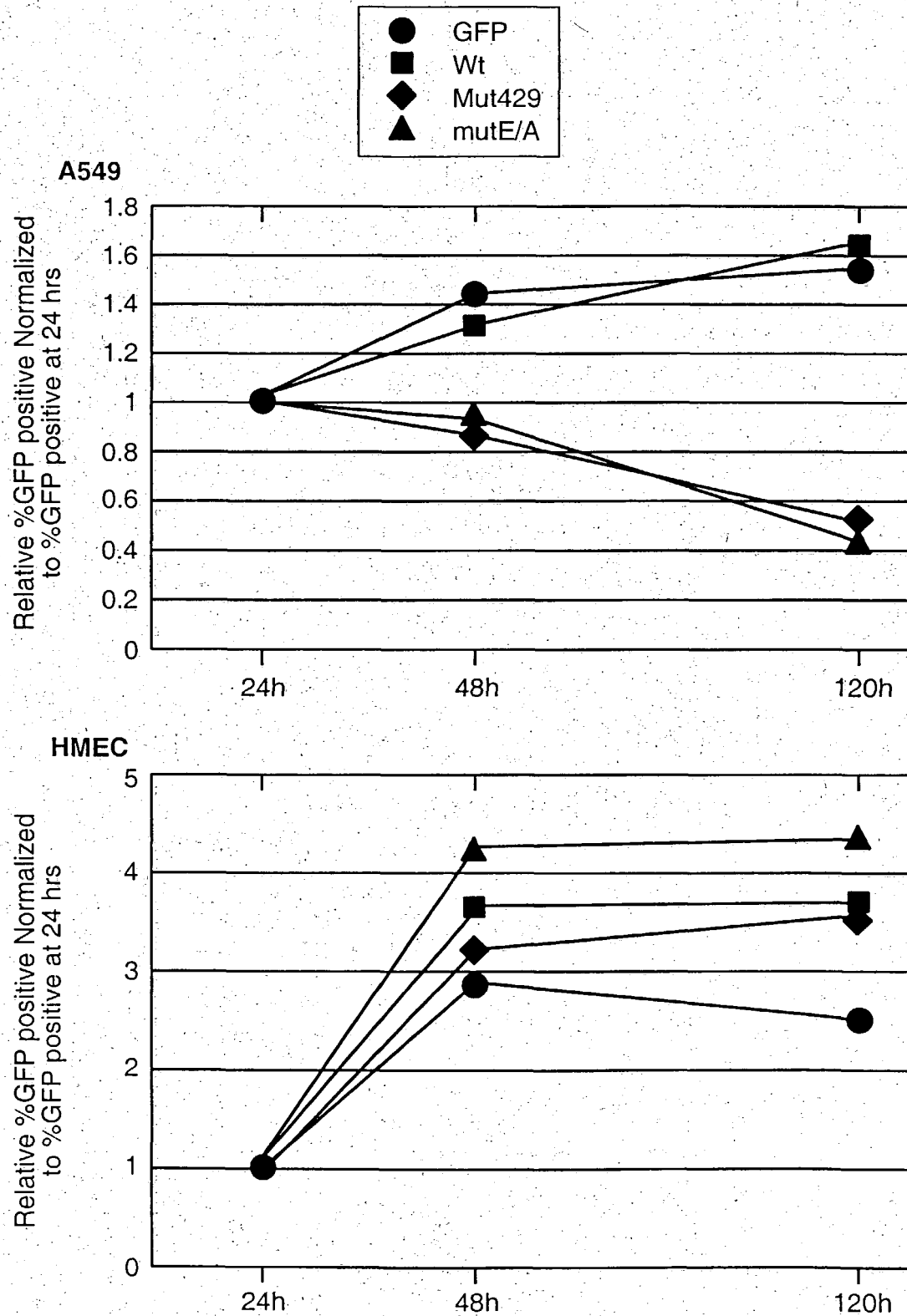


FIG 6B

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**Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells (HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue**



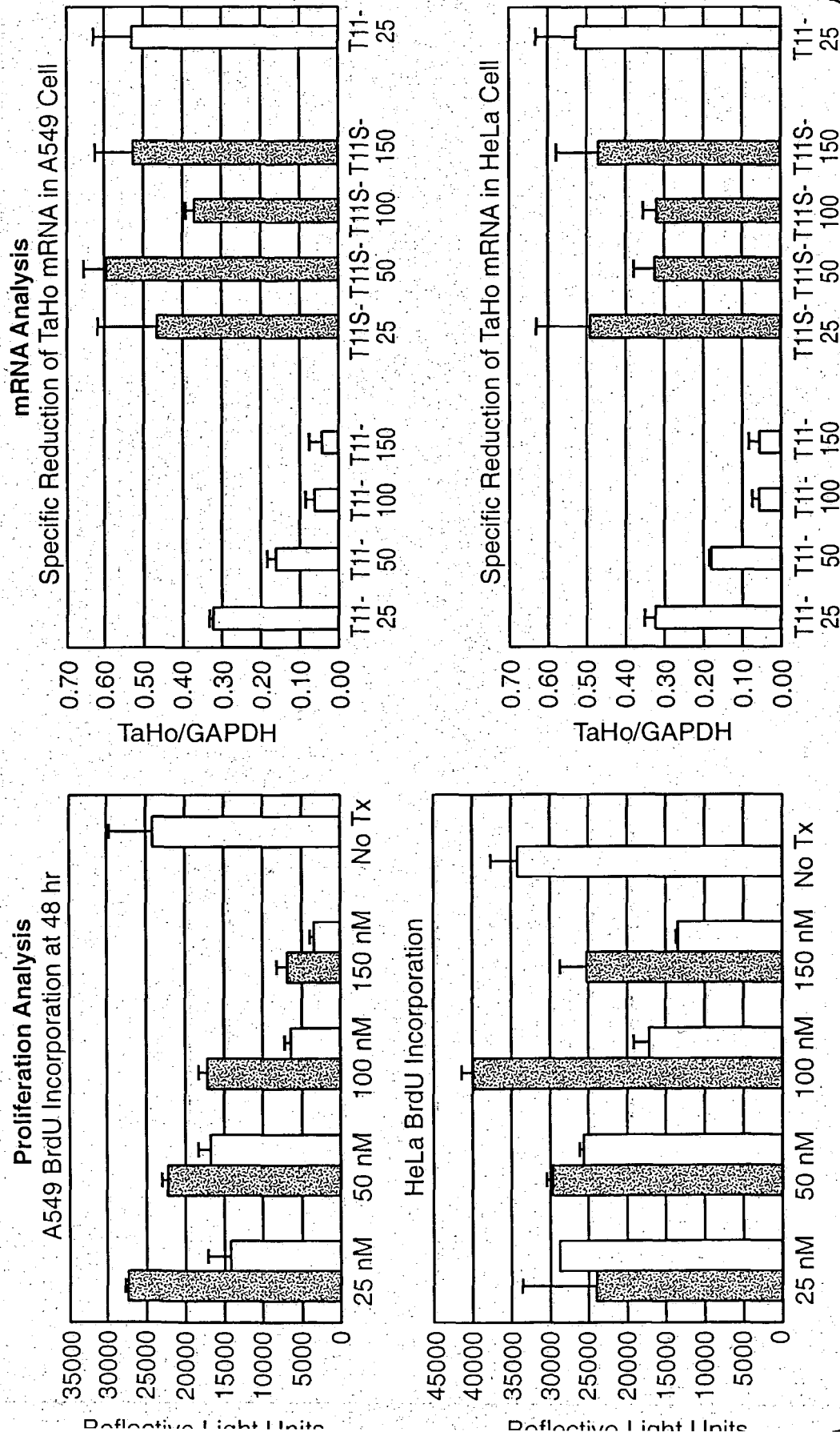
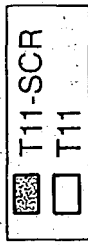


GTGGAACAGAGGTGCTTCC

Tankyrase Homologue	GTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAGGAGGTTCCAGGAGTAGATTTAGCAT	2838
Tankyrase	ATGCAGGGGATGGCGCGCGGGAACAGAAAAGGAAGGAAGTTGCTGGTCTTGACAT	3091

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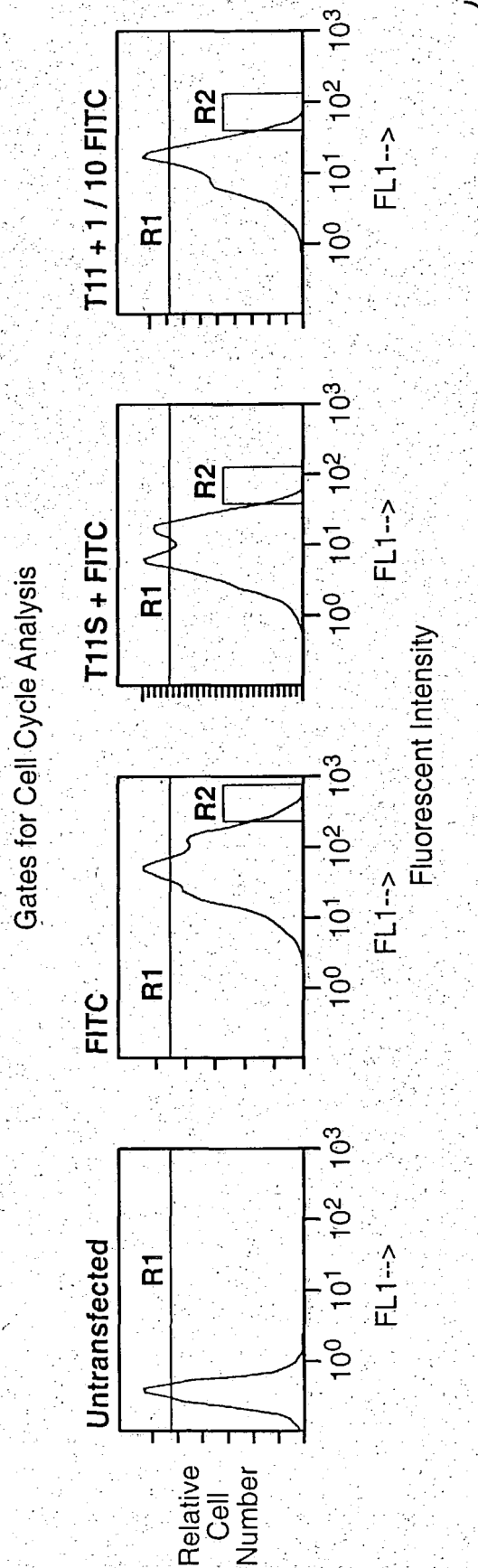
# Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells



**FIG.\_9**

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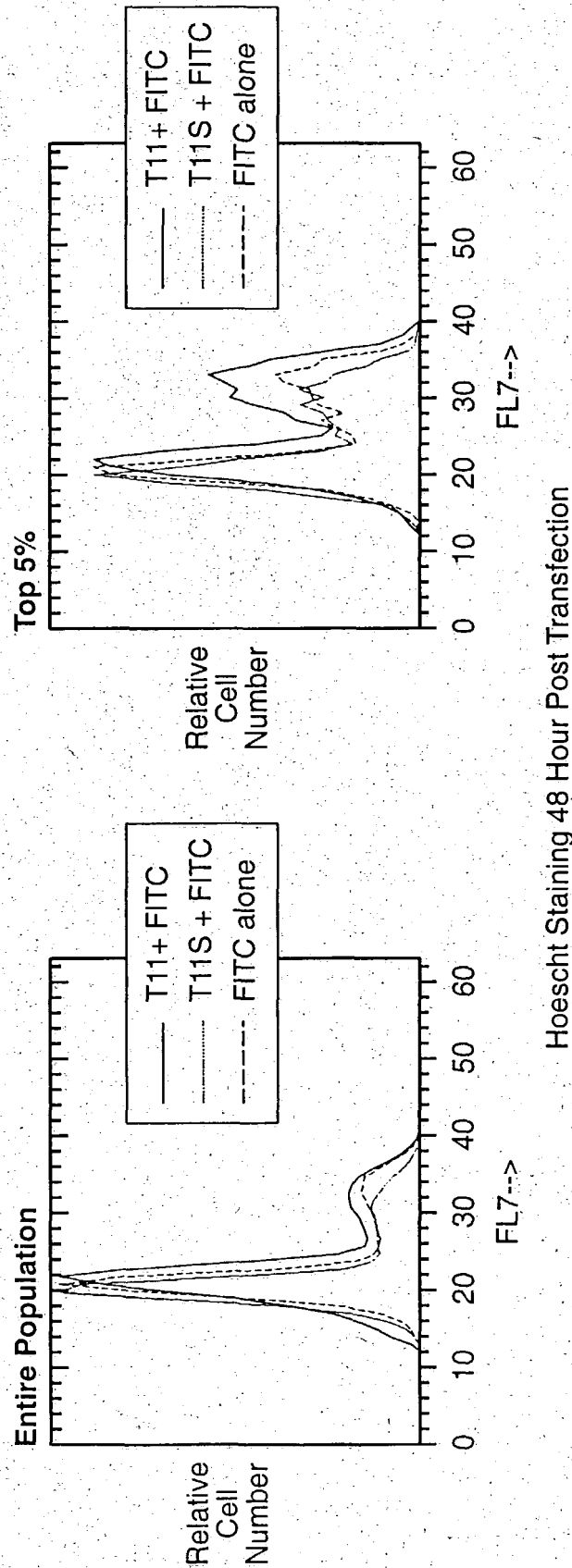
Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC), After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

**FIG. 10A**

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Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC). After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle

## Cell Cycle Analysis

**FIG. 10B**

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mRNA Expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA Expression was Normalized by 90kDa Highly Basic Protein (HBP) and Ribosomal Protein S9 (S9)

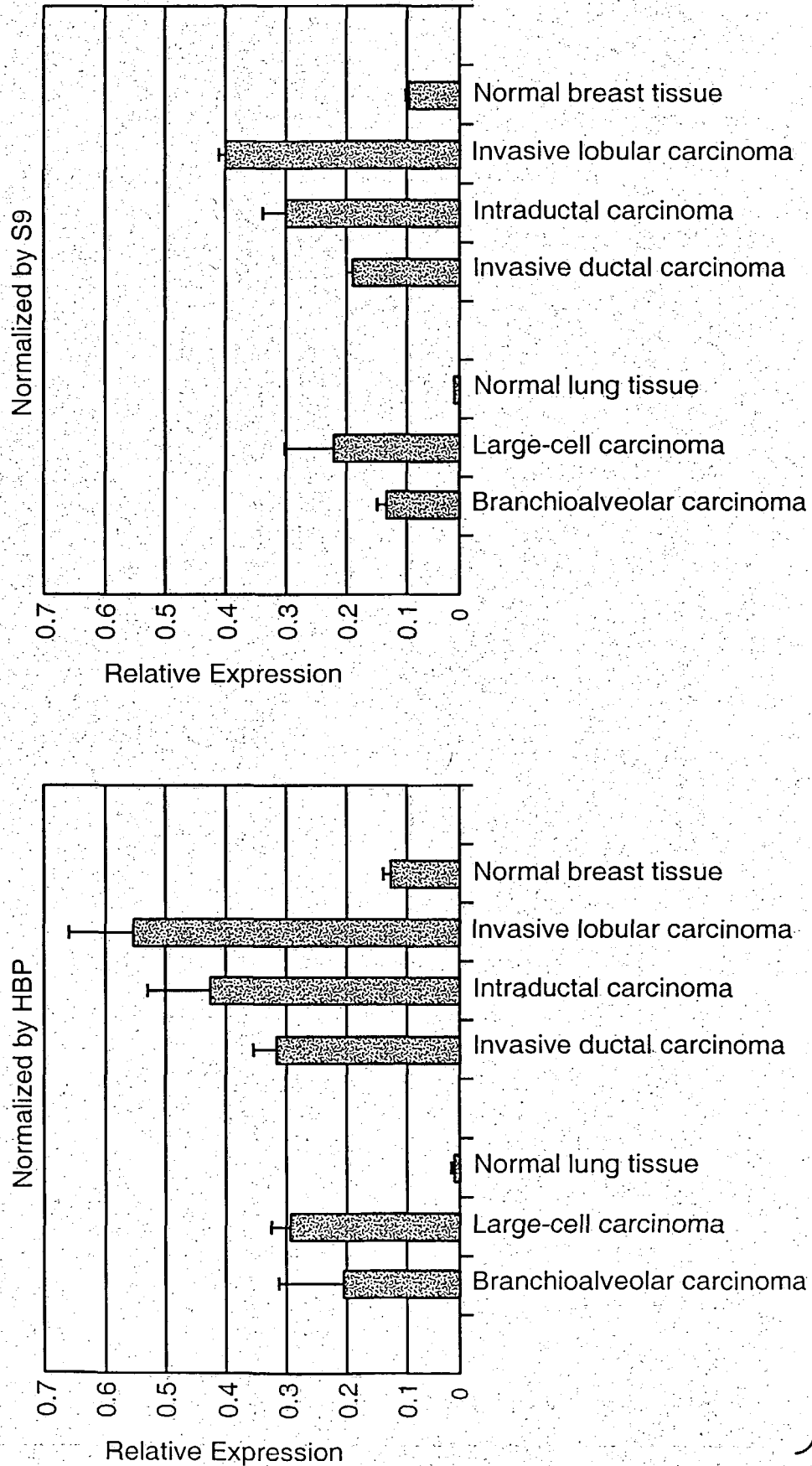


FIG. 11

**Procedure for Nonisotopic Detection of Poly-ADP Ribosylation  
Using Anti-GFP mAb-Coated Plates**

Protein lysates from 293T cells normalized by GFP  
fluorescence and total protein

↓

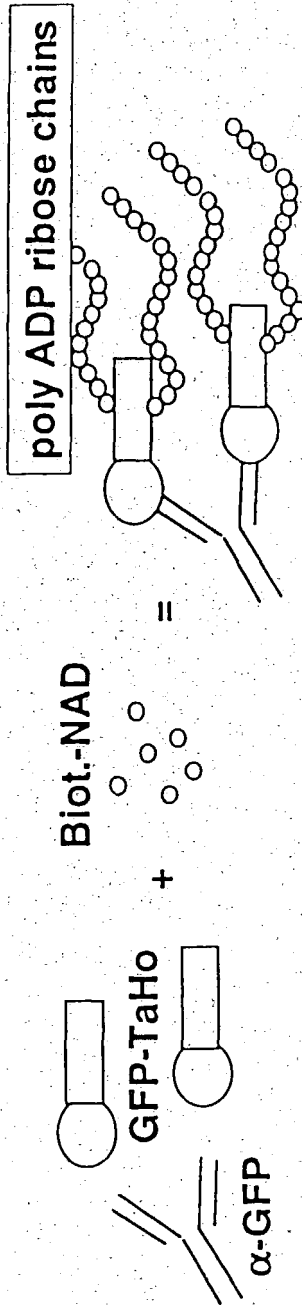
Immobilization of GFP-tankyrase homologue in anti-  
GFP Coated plates

↓

Auto PARP reaction with Biotinylated-NAD in 96 wells

↓

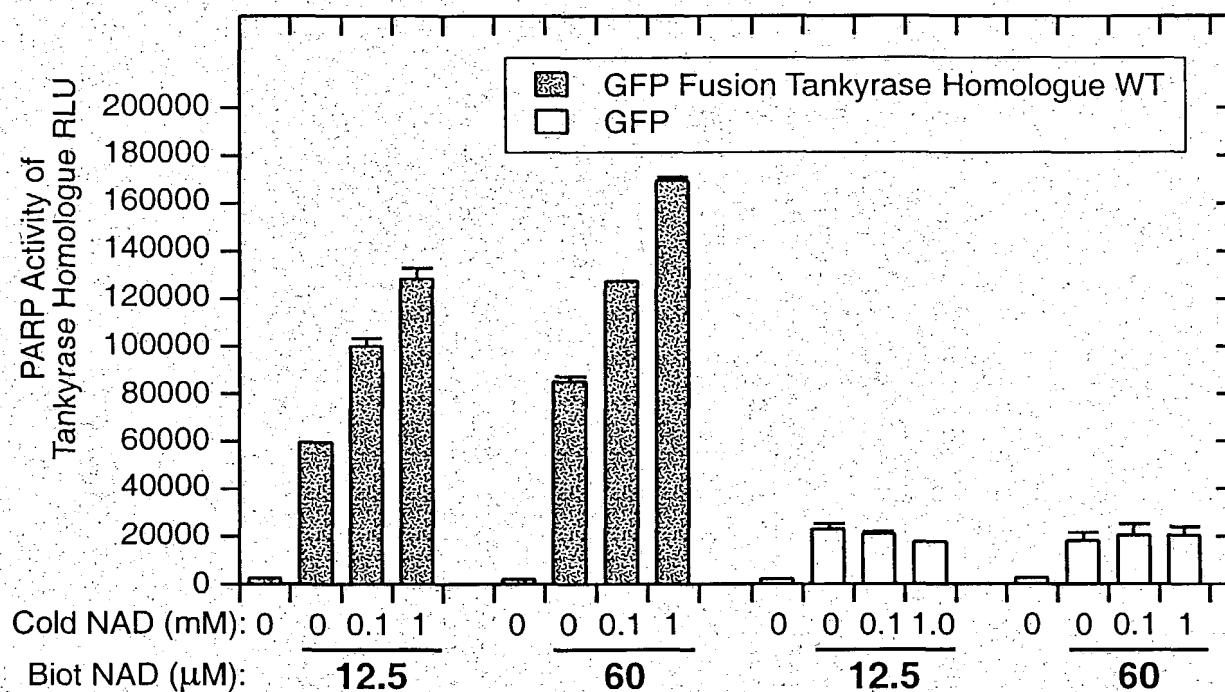
Detection of poly ADP ribose chains with Streptavidin-  
HRP and chemiluminescent substrate



**FIG.\_12**



### Non-Isotopic Plate-Based Detection of TaHo PARP Activity in the Presence of Biotinylated NAD



**FIG. 13**

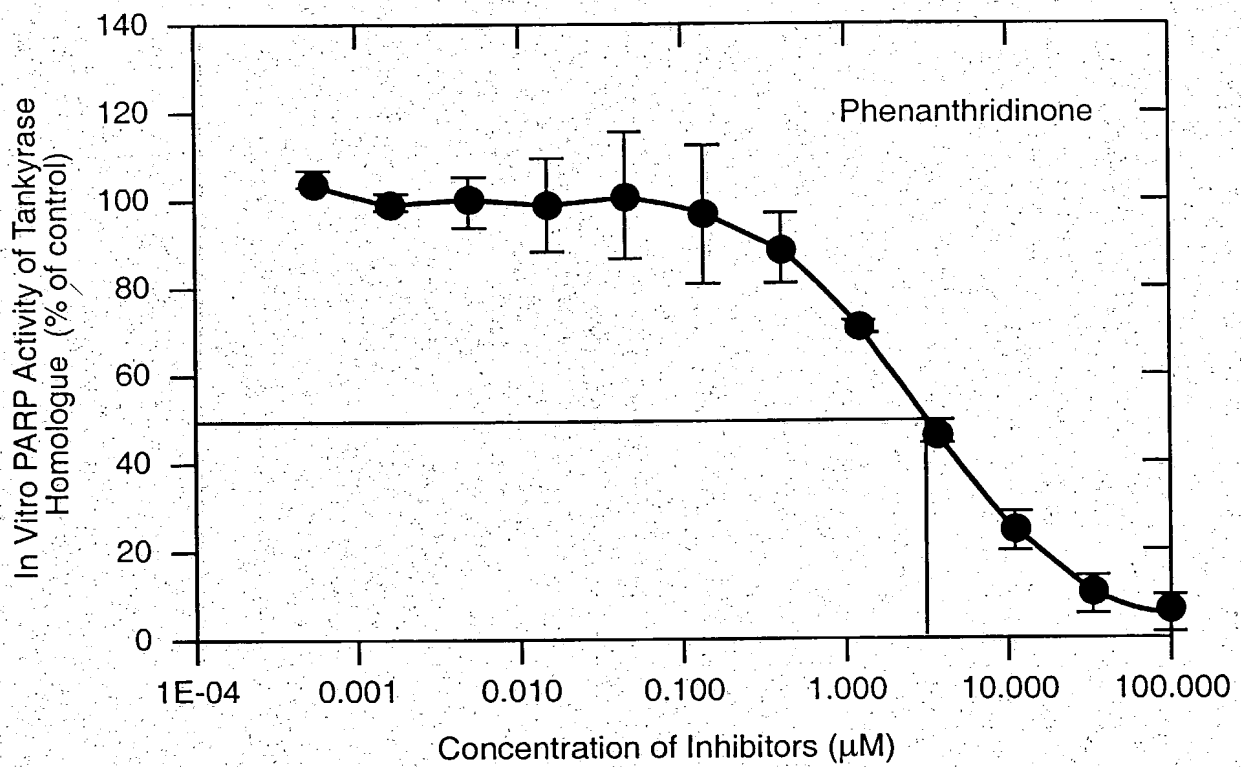
### Comparison of IC<sub>50</sub> Values of the PARP Inhibitors

	Approximate IC <sub>50</sub> (nM)	hPARP assay IC <sub>50</sub> (nM)		
	TaHo	Rigel	Decker*	Rankin*
3AB	>50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	>50 000	30 000	>>5 000	31 000

\* Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172

\* Rankin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317

### Inhibition of Tankyrase Homologue PARP Activity by hPARP Inhibitors

**FIG.\_15****FIG.\_16***FIG.\_16A**FIG.\_16B**FIG.\_16C*

# H-1: Tankyrase Homologue isoform-1, TH-2: Tankyrase Homologue isoform-2 1 (Red): the first methionine in the sequence, Z: stop codon n this figure, the first methionine in TH-1 sequence is position 1 (M1)

FIG.-16A

aho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because  
 f frame shift.

aho F/L mutant has the mutation at position 871

aho E/A dC mutant has the mutation at position 948, ends at position 957 (A) and adds 2  
 mino acids.

H-1	-----	
H-2		RCSARRGAAGGQGAQRGARVGA AHGTAPDPVTAGSQ -231
H-1	-----	
H-2		AARALSASSPGGLALLAGPGLLLRLLALLAVAAARIMSGRRRCAGGGAACASAAAEAVE -171
H-1	-----	
H-2		PAARELFEACRNGDVERVKRLVTPEKVNRSRDTAGRKSTPLHFAAGFGRKDVVEYLLQNGA -111
	Ankyrin repeat	Ankyrin repeat
H-1	SVQARDDGGLIPLHNACSFSGHAEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV -51	
H-2	NVQARDDGGLIPLHNACSFSGHAEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV -51	
	Ankyrin repeat	Ankyrin repeat
		•TH1 start
H-1	LLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV 10	
H-2	LLQHGAETIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV 10	

# FIG. 16B

TH-1	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-2	NCHASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVT	EL 70	
	NCHASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVT	EL 70	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	LVKHGACVNAMEDLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSAIDLAPTQ	L 130	
TH-2	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	KERLAYEFKGHSLQAAREADVTRIKKHLSEMVNFKHPQTHETALHCAAA	SPYPRKQI 190	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	CELLLRKGANINEKTEFLTPLHVASEKAHNDVVEVVVKHEAKVNALDNLGQTS	LHRAAY 250	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	CGHLQTCRLLLSYGCDPNIISLQGTALQMGNEENVQQLQEGISLGNSEAD	RQLLEAKA 310	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	GDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHGADV	HAKDKGGLVP 370	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
TH-1	LHNACSYGHYEVAELLVKHGAVNVNADLWKFTPLHEAAAKGKYEICKLL	LQHGADPTKKN 430	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat
	GMEILLWILLKMEIQIFKICLGEMQLCZ		
TH-1	RDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKLSSPDNVNCR	DTQGRHSTP 490	
	_____	_____	_____
	Ankyrin repeat	Ankyrin repeat	Ankyrin repeat

T

Deletion--•

# FIG.-16C

TH-1 LHLAAGYNNLEVAEYLLQHGADVNAQDKGLIPLHNAASYGHVDVAALLIKYNACVNATD 550  
 Ankyrin repeat Ankyrin repeat

TH-1 KWAFTPLHEAAQKGRQTQCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSA 610  
 Ankyrin repeat Ankyrin repeat

TH-1 LPSCYKPOVLNGVRSPGATADALSSGPPSSSLSAASSLDNLGSFSELSSVVSSSGTEG 670  
 Ankyrin repeat

TH-1 ASSLEKKE--VPGVDFSITQFVRNLGLEHLMDFEREQITLDVLVEMGHKELKEIGINAY 730  
 SAM domain

TH-1 GHRHKLIGVERLISGQQLNPYLTLNTSGSGTILIDLSPDDKEFQSVSEEMQSTVREHR 790

TH-1 DGGHAGGIFNRYNLIKQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNAIL 850

TH-1 HKGFDERHAYIGMFGAGIYFAENSSKSNQYVYIGGGTGCPVHKDRSCYICHRQLLFGR 910  
 • F→L mutation  
 PARP domain

TH-1 VTGKSFLQFSAMKMAHSPPGHSHVTGRPSVNGLALEYVIYRGEQAYPEYLITYQIMRP 970  
 • E→A • Deletion.

TH-1 EGMVDG 976